

Cardiovascular effects of weight reduction in obese patients with angina pectoris¹

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Reduction in body weight to normal limits by dietary restriction over a period of one year did not result in any symptomatic, electrocardiographic, or haemodynamic improvement in 6 obese patients with exercise-induced angina pectoris. Over the same period there was no symptomatic or objective evidence of cardiac deterioration in 4 similar patients who failed to reduce weight.

Weight reduction is frequently advised in obese patients with ischaemic heart disease, particularly those suffering from exercise-induced angina pectoris. Whatever the assumptions on which such advice is based, there is little objective information available of the effects of weight reduction on the symptoms or electrocardiographic signs of myocardial ischaemia or on the abnormal function of the heart in these patients. Furthermore, there are reports that suggest that starvation may exert deleterious effects on the heart both in healthy subjects (Garnett *et al.*, 1969; Sandhofer *et al.*, 1973) and in patients with pre-existing heart disease (Cubberley, Polster, and Schulman, 1965; Spencer, 1968). For these reasons the following

study was designed to determine the effects of chronic dietary restriction in obese patients with otherwise uncomplicated angina pectoris.

Subjects and methods

Ten male patients, average age 52 years (range 42 to 62), with uncomplicated exercise-induced angina pectoris were studied (Table 1). Angina had been present for 1 to 10 years and was stable. None had had a myocardial infarction, none had hypertension or diabetes, and none had evidence of other heart disease. All were in sinus rhythm.

The resting electrocardiogram was normal in all patients but during treadmill walking the ST segment in chest lead V₅ was depressed by more than 0.1 mV from the isoelectric line and showed the pattern of ischaemic configuration (Thadani *et al.*, 1973). The chest radiograph was normal and the cardiothoracic ratio less than 50 per cent in all. Cineangiograms showed a normal sized left ventricular cavity without mitral valve incompetence; selective coronary angiograms showed extensive atheromatous involvement of two or more coronary arteries with reduction of the arterial diameter by 50 per cent or more.

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TABLE 1 *Effects of dietary restriction in obese patients with angina pectoris*

Dietary achievement	Age (yr)	Height (cm)	Initial weight (kg)	Weight* excess (kg)	Weight loss (kg)
Group 1 - success (6)	50 ± 3	176 ± 2	95.7 ± 3.4	18.3 ± 1.7	16.3 ± 1.8
Group 2 - failure (4)	48 ± 4	174 ± 3	97.1 ± 2.8	19.9 ± 2.3	0.5 ± 0.3

Data given as mean ± standard error of mean.

Number in parentheses relate to number of patients in each group.

* *Documenta Geigy, Scientific Tables*, 6th ed. Ed. by Konrad Dien, Geigy Pharmaceutical Company, Manchester, 1962.

All patients were under consideration for coronary artery bypass surgery. The scientific reasons for the study, the proposed programme of investigation, its relation to their individual treatment, and the possible wider therapeutic implications of the results were explained to each patient. The voluntary nature of their co-operation both with the diagnostic procedures and the dietary regimen was particularly emphasized; without inducement all freely consented to the programme of study (Medical Research Council, 1964; Ormrod, 1968).

Design of investigation

Patients were trained to walk on a treadmill and also to exercise in the supine position on a bicycle ergometer at constant speed and load. Levels of exercise were selected to induce anginal pain at about the third minute of walking or bicycle exercise. Patients indicated the onset and duration of pain by a finger-operated light switch without prompting. Training was carried out two hours or more after a light meal and patients were asked not to smoke during this time. It was continued until the onset of pain was repeatable to within 20 seconds, usually after 3 to 5 sessions.

There were two separate studies in each patient. The first study was designed to determine the time of onset and resolution of angina and the accompanying electrocardiographic abnormalities during treadmill walking (speed 1 to 2 m.p.h., 1 to 10° incline). Exercise was stopped immediately the patient indicated the presence of anginal pain. Diagnostic haemodynamic investigations were undertaken separately under conventional catheter conditions. Measurements began 30 minutes after catheters had been introduced into the pulmonary artery, aorta, and left ventricle. Electrocardiogram, intravascular pressures, and cardiac output were recorded during a four-minute resting period. Supine bicycle leg exercise was then started; electrocardiogram and intravascular pressures were recorded continuously and the cardiac output measured by the direct oxygen Fick method during the last two minutes of exercise after the onset of anginal pain.

After these studies, patients started on an 800 to 1000 calorie low-fat diet and were then discharged home. Medication was restricted to sublingual glyceryl trinitrate. No exercise programme was instituted. Patients were reviewed at monthly intervals; no progressive increase in anginal pain or changes in electrocardiographic severity of myocardial ischaemia during exercise were noted in any patient. After 12 months of dietary restriction, 6 patients had reduced to within 4 per cent of their 'ideal' weight and 4 had failed to lose weight.

Patients were then readmitted to hospital for reconsideration for coronary artery surgery. Selective coronary arterial and left ventricular cineangiographic studies were undertaken; the comparative electrocardiographic and haemodynamic studies were carried out immediately before angiography.

Laboratory techniques, measurements, and statistical methods

The laboratory methods employed in these studies have been described in detail elsewhere (Sharma *et al.*, 1972). Using haemodynamic methods similar to those in the present study, duplicate measurements of oxygen uptake, cardiac output, intravascular pressures, and left ventricular end-diastolic pressure varied within 5, 7, 3, and 8 per cent, respectively, of the mean value. The electrocardiograph was recorded with disc adhesive electrode (Dracard Ltd.) from chest lead V₅ and calibrated externally (0.1 mV = 1.0 mm). ST segment depression was measured in this lead from the J point to the isoelectric line joining two consecutive PR intervals (Thadani *et al.*, 1973); measurements were averaged over five consecutive beats with a stable isoelectric baseline. Measurements were recorded on an ultra-violet light recorder (S.E. Model 3012) using only the linear arc of traverse of the galvanometers. Patients were always weighed on the same scales which were calibrated by standard brass weights.

Probability of statistical significance of changes was calculated by Student's 't' test for paired data.

Results

Both studies were accomplished without untoward incident in all patients.

Reduction in body weight (Table 1)

The initial body weight of the 6 patients in group 1 who achieved weight reduction exceeded the actuarial ideal by an average of 24 per cent (range 21 to 32). After dieting, during which the average weight loss was 16.3 kg, the average excess body weight had been reduced to 3 per cent (range 2 to 4).

In 4 patients (group 2) 12 months of dietary advice failed to achieve any sustained reduction in body weight.

Effect on symptoms (Table 2)

a) Treadmill walking There was no consistent change in the time of onset, duration, or character of the anginal pain at the same walking speed and treadmill incline in patients of either group.

b) Supine bicycle exercise There was no consistent change in time of onset, duration, or character of the anginal pain during supine leg exercise in patients of either group.

Effect on electrocardiogram (Table 3)

There was no consistent change in electrocardiographic ST segment depression or T wave height during both forms of exercise either in patients who had reduced weight or in those who had not.

TABLE 2 Effects of dietary restriction on anginal symptoms

Dietary achievement	Treadmill walking				Supine bicycle exercise			
	Before*		After†		Before		After	
	Onset‡	Resolution§	Onset	Resolution	Onset	Resolution	Onset	Resolution
Group 1 – Success	164 ± 21	187 ± 14	171 ± 13	197 ± 12	147 ± 28	206 ± 23	158 ± 18	228 ± 31
Group 2 – Failure	186 ± 17	203 ± 20	200 ± 31	156 ± 19	171 ± 22	251 ± 19	206 ± 24	191 ± 27

Data given as mean ± standard error of mean.

* Before dietary restriction.

† After dietary restriction.

‡ Time of onset of anginal pain in seconds after start of exercise.

§ Time of resolution of anginal pain after stopping exercise.

TABLE 3 Effects of dietary restriction on electrocardiographic evidence of left ventricular ischaemia during exercise

Dietary achievement	Variable	Treadmill walking		Supine bicycle exercise	
		Before*	After†	Before	After
Group 1 – Success	J-ST‡	2.1 ± 0.1	2.2 ± 0.2	2.7 ± 0.3	2.6 ± 0.5
	T wave§	2.5 ± 0.3	2.5 ± 0.4	2.9 ± 0.5	2.6 ± 0.3
Group 2 – Failure	J-ST	2.3 ± 0.2	2.1 ± 0.3	2.5 ± 0.2	2.7 ± 0.3
	T wave	2.7 ± 0.4	2.6 ± 0.2	3.3 ± 0.4	3.4 ± 0.5

Data given as mean ± standard error of mean.

* Before dietary restriction.

† After dietary restriction.

‡ Depression of ST segment (mm) from isoelectric line at J point.

§ Maximum height of T wave above isoelectric line.

TABLE 4 Haemodynamic effects of dietary restriction in obese patients with exercise induced angina pectoris

Variable	Group 1 – success (6)				Group 2 – failure (4)			
	Before*		After†		Before		After	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
Respiratory rate (per min)	16 ± 2	29 ± 3	17 ± 2	26 ± 3	17 ± 1	26 ± 1	15 ± 2	27 ± 2
Ventilation (l./min per m ²)	4.5 ± 0.4	14.9 ± 1.1	4.2 ± 0.7	14.0 ± 1.2	4.9 ± 0.4	14.1 ± 0.9	5.1 ± 0.6	16.0 ± 1.3
Oxygen uptake (ml/min per m ²)	135 ± 6	590 ± 25	120 ± 4	540 ± 35	131 ± 9	597 ± 24	133 ± 6	583 ± 31
Cardiac output (l./min per m ²)	2.2 ± 0.1	5.3 ± 0.3	2.3 ± 0.2	5.4 ± 0.5	2.4 ± 0.2	5.8 ± 0.4	2.3 ± 0.2	5.6 ± 0.3
Heart rate/min	79 ± 4	122 ± 6	75 ± 4	125 ± 8	75 ± 3	129 ± 6	81 ± 4	124 ± 4
Systemic arterial mean pressure (mmHg)	115 ± 4	146 ± 8	113 ± 5	141 ± 9	111 ± 5	137 ± 9	106 ± 3	134 ± 8
Left ventricular systolic pressure (mmHg)	134 ± 6	170 ± 8	133 ± 7	161 ± 12	132 ± 5	161 ± 8	128 ± 7	158 ± 7
Left ventricular end-diastolic pressure (mmHg)	12 ± 1	37 ± 5	13 ± 1	39 ± 3	14 ± 1	41 ± 6	12 ± 2	38 ± 3

Data given as mean ± standard error of mean.

Numbers in parentheses relate to numbers of patients in each group.

* Before dietary restriction.

† After dietary restriction.

Effect on left ventricular function (Table 4)

Dietary restriction was not associated with any significant change in any of the measured variables of left ventricular function in any patient whether weight reduction was achieved or not. There was a decrease in total body oxygen uptake proportional to the reduction in body weight, both at rest and during exercise, in patients who reduced weight. In these patients there was an increase in systemic blood flow per unit body mass (cardiac output per kg body weight), ($P < 0.05$).

Discussion

These results demonstrate that the reduction of body weight by dietary restriction had no immediate effect on symptoms, electrocardiographic signs, or haemodynamic evidence of myocardial ischaemia in obese patients with exercise-induced angina pectoris. Likewise, over the same period there was no subjective or objective evidence of further progress of the disease in similar obese patients who failed to reduce weight.

In order to place these results in clinical perspective, the limitations imposed by the choice of the patients, design of the study, and investigative techniques used must be outlined. The patients selected for study were suffering from moderate obesity; body weight was increased by an average of 24 per cent. Though they probably represent the range of obesity most commonly encountered in clinical practice, it is possible that a greater reduction in weight in more obese subjects may have been associated with more symptomatic and objective evidence of benefit. None of these patients had hypertension or diabetes and none had a history of myocardial infarction; it is possible that reduction of obesity in patients with angina complicated by one or more of these factors may be of more benefit than in those selected for the present study. However, it is reasonable to expect that if angina was to be relieved by weight reduction, it would be in this type of patient in whom pain was induced solely by exercise, and not in those in whom angina was precipitated by other stimuli, e.g. emotion. It must also be pointed out that the symptomatic evaluation in these patients was measured under strict laboratory conditions employing a standardized exercise test. It was not concerned with a subjective evaluation based on an historical account of the number of anginal attacks or the number of glycerol trinitrate tablets consumed. Whatever may be the relevance of these latter assessments, they are almost certainly less reliable indices of improvement in patients with angina pectoris than the results of the standardized exercise tests used in the present study.

The natural history of the disease may have progressed during the course of the study, and the fact that no symptomatic, electrocardiographic, or haemodynamic change was demonstrated over this period does not necessarily imply that the reduction of obesity had no beneficial effect. It may simply have prevented the deterioration that may have otherwise occurred. Though this argument cannot be conclusively refuted from the present evidence, in patients who achieved weight reduction the angina had been clinically 'stable' for many months beforehand, and in the 'control' group of patients who did not reduce weight there was no progression of symptoms, electrocardiographic, or haemodynamic changes over the same period. It is also important to point out that this study was not designed to answer the more difficult question as to the possible effects of maintained weight reduction; it was specifically concerned with the immediate effects of reduction of obesity. Neither were possible changes in cardiac metabolism associated with dietary restriction and weight reduction studied. But within these limitations, the results clearly indicate that whatever may be the advantages of weight reduction in obese patients with exercise-induced angina pectoris, they do not include symptomatic, electrocardiographic, or haemodynamic evidence of immediate improvement.

There is little doubt that obesity is related to an increased incidence of ischaemic heart disease; there is a distinct relation between body weight relative to ideal weight and the risk of developing angina pectoris (Kannel *et al.*, 1967). However, it is equally important to emphasize that there is no evidence that *reduction* in obesity lessens this incidence. Though more extensive studies are necessary before such an important therapeutic relation is established, the results of the present investigation indicate that the correlation may not be as simple as first supposed.

These observations also raise the important issue as to whether there are any possible contraindications to chronic dietary restriction in ischaemic heart disease. Though this question cannot be answered with certainty, evidence is accumulating that starvation may be harmful in such patients. Though total starvation has been maintained in obese but otherwise healthy patients for periods of up to 249 days without complication (Thomson, Runcie, and Miller, 1966), there have been a number of reports of sudden deaths associated with severe dietary restriction both in healthy subjects (Garnett *et al.*, 1969; Sandhofer *et al.*, 1973) and in obese patients with pre-existing heart disease (Cubberley *et al.*, 1965; Spencer, 1968). Though the cause of these sudden deaths is unknown, it is

interesting to speculate that the severe carbohydrate restriction enforced in all slimming diets may be implicated. There is abundant evidence of the importance of glucose in sustaining the metabolism (Scheuer, 1967; Opie, 1972), contractile activity (Taylor, 1971; Taylor and Majid, 1971; Majid *et al.*, 1972), and survival of hypoxic myocardium (Weissler *et al.*, 1968; Maroko *et al.*, 1972). In angina pectoris an increase in the blood sugar level significantly lessens electrocardiographic evidence of myocardial ischaemia (Sharma, Majid, and Taylor, 1974), while hypoglycaemia is liable to precipitate chest pain (Smith, 1933; Friedberg, 1966). It is not unreasonable to suppose, therefore, that the reduced availability of glucose during chronic starvation may further impair myocardial metabolism in patients with angina pectoris. It is also possible that this state of affairs may be aggravated by the hypoglycaemic activity of the beta-receptor blocking drugs with which these patients are often concurrently treated (Byers and Friedman, 1966; Kotler, Berman, and Rubenstein, 1966; Abramson, Arky, and Woeber, 1966).

Though these limited studies need more extensive confirmation, they serve to indicate that the simple correction of obesity in patients with angina pectoris may not result in any measurable symptomatic relief or objective benefit to the patient. Indeed, if strict dieting is enforced it may possibly be deleterious to his well-being. Moreover, the possible therapeutic interaction between dietary restriction and the beta-blocking drugs suggests that caution should be exercised in their concurrent use in patients with angina pectoris.

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